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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/759,595	01/11/2001	Holger Wesche	018781-003910US	9425

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EXAMINER	
MURPHY, JOSEPH F	

ART UNIT	PAPER NUMBER
1646	20

DATE MAILED: 09/05/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application N .	Applicant(s)	
	09/759,595	WESCHE ET AL.	
	Examiner	Art Unit	
	Joseph F Murphy	1646	

-- The MAILING DATE f this communication appears n the c ver sheet with the c rresp ndence address --

Peri d for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 May 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disp sition of Claims

4)☒ Claim(s) *1-4,6-15,31,63 and 67* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,6-9,11-15,31,63 and 67* is/are rejected.

7)☒ Claim(s) *4 and 10* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Formal Matters

Claims 1, 31 were amended, claims 5, 16-30, 32-62, 64-66 were cancelled, and new claim 67 was added in Paper No. 19, 5/16/2003. Claims 1-4, 6-15, 31, 63, 67 are pending and under consideration.

Response to Amendment and Arguments

Applicant's arguments filed in Paper No. 19, 5/16/2003 have been fully considered but they are persuasive in part, for the reasons set forth below.

The rejection of claims 4 and 10 under 35 U.S.C. 112, first paragraph have been withdrawn based on Applicant's arguments.

The rejection of claim 12 under 35 USC 112 second paragraph has been withdrawn based on Applicant's arguments.

Claim Rejections - 35 USC § 112 first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-3, 6-9, 11-15, 31, 63 stand rejected, and new claim 67 is rejected, under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a nucleic acid encoding an amino acid of SEQ ID NO: 1, or a nucleic acid with the sequence as set forth in SEQ ID NO: 2, does not reasonably provide enablement for a nucleic acid encoding an amino acid which is a subsequence of SEQ ID NO: 2, or a nucleic acid which encodes a polypeptide which is 98% identical to SEQ ID NO: 1, a nucleic acid encoding an amino acid which is a

subsequence of a polypeptide which is 98% identical to SEQ ID NO: 2, for reasons of record set forth in Paper No. 18, 2/10/2003. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Claims 1-15, 31 and 63 are overly broad since insufficient guidance is provided as to which of the myriad of variant nucleic acids encode polypeptides which will retain the characteristics of IRAK-4. Applicants do not disclose any actual or prophetic examples on expected performance parameters of any of the possible muteins of IRAK-4. It is known in the art that even single amino acid changes or differences in the amino acid sequence of a protein can have dramatic effects on the protein's function. It is also known in the art that a single amino acid change in a protein's sequence can drastically affect the structure of the protein and the architecture of an entire cell. For example, Voet et al. (1990) teaches that a single Glu to Val substitution in the beta subunit of hemoglobin causes the hemoglobin molecules to associate with one another in such a manner that, in homozygous individuals, erythrocytes are altered from their normal discoid shape and assume the sickle shape characteristic of sickle-cell anemia, causing hemolytic anemia and blood flow blockages (pages 126-128, section 6-3A and page 230, column 2, first paragraph).

Since the claims encompass variant nucleic acids and given the art recognized unpredictability of the effect of mutations on protein function, it would require undue experimentation to make and use the claimed invention. Given the breadth of claims 1-15, 31 and 63 in light of the predictability of the art as determined by the number of working examples, the level of skill of the artisan, and the guidance provided in the instant specification and the

prior art of record, it would require undue experimentation for one of ordinary skill in the art to make and use the claimed invention.

Applicant argues that the claims as amended recite a functional limitation characteristic of IRAK-4, and that this function is easily tested. However, the functional limitation added to the claims, which now recites that the encoded polypeptide must have "IL-1R/Toll family member signal transduction activity" is not clear, as set forth in the rejection under 35 USC 112 second paragraph, infra. The term "IL-1R/Toll family member signal transduction activity" is vague and indefinite because it is not clearly defined in the specification. In the amendment to the specification in Paper No. 7, 10/18/2001, it is set forth that the Toll receptor shares homology with the IL1 receptor, and that serine/threonine kinases act downstream of Toll activation, and that Toll activation results in the activation of the transcription factor Dorsal, which is homologous to NF-kappaB. Additionally, the specification sets forth that there are diseases associated with IL-1/Toll activity including many types of inflammatory diseases (Specification at 10). Thus the skilled artisan would not be apprised of the metes and bounds of the functional limitation with regard to IRAK-4 activity, since the functional limitation encompasses functions of proteins other than IRAK-4, given that the term "IL-1R/Toll family member signal transduction activity" encompasses such disparate and unrelated activities as serine/threonine kinase activity, transcriptional factor activity and also inflammatory pathologies. There is not a correlation between the encompassed nucleic acids encoding polypeptide homologous to IRAK-4, when the possible responses which the encoded polypeptide must produce are indefinite. Furthermore, the prior art does not provide compensatory structural or correlative teachings sufficient to enable one of skill to isolate and identify the nucleic acids encompassed: there is no

guidance in the art as to what the defining characteristics of the polypeptides homologous to IRAK-4 might be. Thus, no identifying characteristics or properties of the instant nucleic acids are provided such that one of skill would be able to make and use the encompassed molecules as claimed.

Claims 1-3, 6-9, 11-15, 31, 63 stand rejected, and new claim 67 is rejected, under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention, for reasons of record set forth in Paper No. 18, 2/10/2003. Applicant is directed to the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

These are genus claims. The claims are drawn to a nucleic acid encoding an amino acid which is a subsequence of SEQ ID NO: 2, or a nucleic acid which encodes a polypeptide which is 98% identical to SEQ ID NO: 1, a nucleic acid encoding an amino acid which is a subsequence of a polypeptide which is 98% identical to SEQ ID NO: 2. The specification and claim do not indicate what distinguishing attributes shared by the members of the genus. Thus, the scope of the claim includes numerous structural variants, and the genus is highly variant because a significant number of structural differences between genus members is permitted. The specification and claim do not provide any guidance as to what changes should be made.

Structural features that could distinguish compounds in the genus from others in the protein class are missing from the disclosure. No common structural attributes identify the members of the genus. The general knowledge and level of skill in the art do not supplement the omitted description because specific, not general, guidance is what is needed. Since the disclosure fails to describe the common attributes or characteristics that identify members of the genus, and because the genus is highly variant, a nucleic acid with a sequence as set forth in SEQ ID NO: 2, and the polypeptide of SEQ ID NO: 1 is insufficient to describe the genus. One of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus. Thus, applicant was not in possession of the claimed genus.

Applicant argues that the claims have been amended to clarify that the claimed nucleic acid encodes a polypeptide which has IRAK-4 activity, namely the ability to transduce signals from IL-1R/Toll family members, and that based on the direction in the specification, one of skill in the art would be able to recognize polypeptides which retain this function. However, as set forth in the rejection under 35 USC § 112 second paragraph (infra), the claims recite that the encoded polypeptide must have "IL-1R/Toll family member signal transduction activity" is not clear, as set forth in the rejection under 35 USC 112 second paragraph, infra. The term "IL-1R/Toll family member signal transduction activity" is vague and indefinite because it is not clearly defined in the specification. Since the term IL-1R/Toll family member signal transduction activity" encompasses such varying responses including, inter alia, encompasses such disparate and unrelated activities as serine/threonine kinase activity, transcriptional factor activity and also inflammatory pathologies, and that these activities since the functional limitation encompasses functions of proteins other than IRAK-4, there is not a correlation

between the encompassed nucleic acids encoding polypeptides which must have IL-1R/Toll family member signal transduction activity", when the possible responses which the encoded polypeptide must produce are indefinite. Furthermore, the prior art does not provide compensatory structural or correlative teachings sufficient to enable one of skill to isolate and identify the nucleic acids encompassed: there is no guidance in the art as to what the defining characteristics of the polypeptide might be. Thus, no identifying characteristics or properties of the instant nucleic acids are provided such that one of skill would be able to predictably identify the encompassed molecules as being identical to those instantly claimed.

Claim Rejections - 35 USC § 112 second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-3, 6-9, 11-15, 31, 63, 67 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The term "IL-1R/Toll family member signal transduction activity" is vague and indefinite because it is not clearly defined in the specification. In the amendment to the specification in Paper No. 7, 10/18/2001, it is set forth that the Toll receptor shares homology with the IL1 receptor, and that serine/threonine kinases act downstream of Toll activation, and that Toll activation results in the activation of the transcription factor Dorsal, which is homologous to NF-kappaB. Additionally, the specification sets forth that there are diseases associated with IL-1/Toll activity including many types of inflammatory diseases (Specification at 10). Thus the

skilled artisan would not be apprised of the metes and bounds of the functional limitation with regard to IRAK-4 activity, since the functional limitation encompasses functions of proteins other than IRAK-4.

Conclusion

Claims 1-3, 6-9, 11-15, 31, 63, 67 are rejected.

Claims 4 and 10 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joseph F. Murphy whose telephone number is 703-305-7245. The examiner can normally be reached on M-F 7:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler can be reached on 703-308-6564. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-308-0294 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Joseph F. Murphy, Ph. D.
Patent Examiner
Art Unit 1646
August 27, 2003

YVONNE EYLER, PH.D
SUPERVISORY PATENT EXAMINER
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